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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,905	12/10/2003	Nandan P. Koppiker	PC10332C	5794

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
EASTERN POINT ROAD
GROTON, CT 06340

EXAMINER

ROYDS, LESLIE A

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 09/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/731,905	Applicant(s) KOPPIKER ET AL.	
	Examiner Leslie A. Royds	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-34 is/are rejected.
- 7) ☒ Claim(s) 29 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 10/206,615; 09/692,781.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>21 December 2004</u> . | 6) <input type="checkbox"/> Other: _____ |

S.P.

DETAILED ACTION

Claims 17-34 are presented for examination.

Applicant's Amendment and Information Disclosure Statement filed December 21, 2004 have each been received and entered into the application. Accordingly, claim 1 has been cancelled and claim 27 has been amended.

In view of the above amendments, the objection to claim 1 and the rejection of claim 1 under 35 U.S.C. 102(e) are now both moot; and the rejection of claim 27-34 under 35 U.S.C. 112, first paragraph has been withdrawn.

Applicant's submission, at the Examiner's request, of the Information Disclosure Statement previously presented in the parent applications has been received and entered into the application. As reflected by the attached, completed copy of form PTO-1449 (two pages total), the Examiner has considered the cited references.

Allowability of the Instant Claims as Noted in the Previous Office Action

Regrettably, the Examiner hereby withdraws the indicated allowability of present claims 17-26 as indicated in the previous Office Action dated July 6, 2004.

Acknowledgement of the Correction to Inventorship of the Presently Claimed Subject Matter

Applicant's request under 37 C.F.R. 1.48(a)-(c) to correct the inventorship of the present application is acknowledged by the Examiner.

In view of the papers filed December 21, 2004, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the

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inventorship, and accordingly, this application has been corrected in compliance with 37 C.F.R. 1.48(a) and 37 C.F.R. 1.48(c). The inventorship of this application has been changed by deleting Eric B. Grossman as requested under 37 C.F.R. 1.48(a) and by adding Eliot R. Forster as requested under 37 C.F.R. 1.48(c).

Applicant's request to correct inventorship under 37 C.F.R. 1.48(a) and 37 C.F.R. 1.48(c) filed December 21, 2004 was further accompanied by a request under 37 C.F.R. 1.48(b) to delete Steven B. Leichter from the inventorship in this nonprovisional application.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Objection to the Oath/Declaration (New Ground of Objection)

The Examiner has noted the submission of a newly executed declaration by inventors Nandan Koppiker and Eliot Forster accompanying the request under 37 C.F.R. 1.48(a) and 1.48(c) to correct the inventorship of the instant application.

The declaration is objected to for failing to set forth a mailing address for inventor Eliot Forster. It does not identify the city and either state or foreign country of residence of this inventor. The residence information may be provided on either on an application data sheet or supplemental oath or declaration.

Appropriate correction is required.

Objection to the Claims (New Ground of Objection)

Claim 29 is objected to for failing to conclude with a period.

Claim Rejection - 35 USC § 103 (New Ground of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 17-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamasaki et al. (U.S. Patent No. 6,166,219; Issued December 2000, Filed November 1998) in view of Ellis et al. (WO 94/28902; 1994), Singh (WO 98/03167; 1998), Bueno et al. (U.S. Patent No. 6,127,418; Issued October 2000, Filed April 1999) and Stedman's Medical Dictionary (Twenty-Second Edition; 1972).

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Yamasaki et al. teaches a pharmaceutical composition comprising a cGMP PDE5 inhibiting benzimidazole compound of the formula (I) or a pharmaceutically acceptable salt thereof (col.35, line 64-col.36, line 26) in combination with a pharmaceutically acceptable carrier (col.37, line 65-col.38, line 6) and further teaches a method of treating a disorder that is responsive to treatment with a cGMP PDE5 inhibiting compound by administering a cGMP-PDE inhibiting compound of formula (I) or a pharmaceutically acceptable salt thereof (col.35, lines 22-55) in a variable amount depending on the age, condition and type of disorder of the patient to be treated (col.38, lines 16-20). The disclosed composition can be administered orally in the solid form of tablets, granules, powders or capsules or in liquid forms, such as solutions, suspensions, syrups, emulsions or lemonades (col.37, line 65-col.38, line 9). Yamasaki et al. further teaches diabetic neuropathy as a medical condition responsive to treatment with the cGMP PDE5 inhibiting compounds (col.1, lines 14-44, especially line 21).

It is acknowledged that Yamasaki et al. is silent as to the particular IC50 concentration or the selectivity ratio of the inhibitor. However, in light of the fact that the particular type of compounds presently claimed are expressly disclosed in Yamasaki et al. and are recognized to function in the same manner as required by the present claims (col.35, lines 22-55, especially lines 52-53), the IC50 concentration or the selectivity ratio of the inhibitor are not seen to differ between the prior art of Yamasaki et al. and that of the present claims, absent factual evidence to the contrary (see present claims 19-20, 24-25 and 30-31).

The differences between the Yamasaki et al. reference and the presently claimed subject matter lie in that the reference does not teach:

(i) the concomitant administration of gabapentin or pregabalin with the cGMP PDE5 inhibitor or the formulation of gabapentin or pregabalin in combination with the cGMP PDE5 inhibitor in the pharmaceutical composition (see present claims 17, 18, 22, 23, 27, 33 and 34);

(ii) the particular use of sildenafil or its pharmaceutically acceptable salts as the cGMP PDE5 inhibitor (see present claims 21 and 32); and

(iii) the treatment of diabetic polyneuropathy (see present claim 28).

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

(i) It is acknowledged that Yamasaki et al. is silent as to the use of gabapentin or pregabalin in the disclosed composition administered for the treatment of diabetic neuropathy. However, both gabapentin and pregabalin were well known in the art to be useful for the same therapeutic purpose of treating diabetic neuropathy. Singh discloses the use of gabapentin or (S)-3-(aminomethyl)-5-methylhexanoic acid (also known as pregabalin; see Bueno et al., U.S. Patent No. 6,127,418, at col.2, lines 50-55) for the treatment of diabetic neuropathy and further discloses a pharmaceutical composition comprising the active GABA compound in combination with an inert, pharmaceutically acceptable carrier for oral administration to mammals, including humans, suffering from such a condition by administering an effective amount of the compound (page 5, lines 9-19 and page 7, lines 4-20). It would, therefore, have been obvious to a person of ordinary skill in the art to employ either gabapentin or pregabalin in combination with a cGMP PDE5 inhibiting composition as disclosed by Yamasaki et al. because each compound was

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known in the art to be successful for achieving the same therapeutic effect. Motivation to administer both compounds flows logically from the efficacy of each compound in treating diabetic neuropathy as demonstrated in the prior art and further because each compound has been previously administered for this same therapeutic objective. In the absence of evidence to the contrary, it is generally *prima facie* obvious to use in combination two or more agents that have previously been used separately for the same purpose. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA) and MPEP §2144.06.

(ii) It is acknowledged that Yamasaki et al. do not expressly teach the use of the cGMP PDE5 inhibitor sildenafil, or its pharmaceutically acceptable salts thereof, as a compound for treating diabetic neuropathy. However, Yamasaki et al. discloses that diabetic neuropathy is a condition responsive to treatment with a cGMP PDE, particularly a cGMP PDE5, inhibiting compound. In light of such a relationship, it would have been an obvious conclusion to one of ordinary skill in the art that the treatment of a condition known to be responsive to a cGMP PDE5 inhibiting agent would not be solely limited to those compounds disclosed by Yamasaki et al, but that effective treatment of such a condition would have been reasonably expected to occur with any one or more other compounds known to exert the same effect (i.e., the inhibition of cGMP PDE5). Thus, the use of a cGMP PDE5 inhibitor compound, e.g., sildenafil, for the formulation of a pharmaceutical composition administered for the treatment of diabetic neuropathy would have been obvious to, and a matter well within the purview of, the skilled artisan. Ellis et al. teaches the compound 5-[2-ethoxy-5-(4-methyl-1-piperazinylsulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one as a potent and selective inhibitor of cGMP-specific PDE5 (page 7, lines 1-3 and page 9, lines 1-3 of the last

paragraph). The use of such a compound was well known in the art to exert inhibitory effects on cGMP-PDE5 and, therefore, would have been reasonably expected to demonstrate the same, or substantially similar, efficacy in treating diabetic neuropathy, as that shown by the benzimidazole cGMP-PDE inhibiting compounds expressly taught by Yamasaki et al.

(iii) Although the present claims recite the use of a cGMP PDE5 inhibitor compound in combination with gabapentin or pregabalin for the treatment of diabetic polyneuropathy, while the cited references teach diabetic neuropathy, the distinction between diabetic polyneuropathy and diabetic neuropathy is not considered a patentable difference, absent factual evidence or direction to the contrary. The presence of the prefix “poly” amounts to nothing more than a quantification of the number of peripheral nerves that are affected by neuropathy resulting from diabetes. In this regard, Stedman’s Medical Dictionary has been cited (1972; p.1000) to show that polyneuropathy is defined as “a disease process involving a number of peripheral nerves.” Thus, regardless of whether the neuropathic phenomenon affects one or more than one peripheral nerve(s), such does not change the fact that both cGMP PDE5 inhibitor compounds and gabapentin and pregabalin were known in the art for the treatment of diabetic neuropathy, in general. It would logically follow, therefore, that two compounds known to have efficacy in the treatment of diabetic neuropathy occurring in one nerve would also be reasonably suggestive of having efficacy in treating diabetic neuropathy occurring in multiple nerves.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Please reference U.S. Patent No. 6,251,904 to Bunnage et al. (Pirazolopyrimidinone cGMP PDE5 Inhibitors for the Treatment of Sexual Dysfunction; Issued June 2001, Filed September 1999).

Rejection of claims 17-34 is deemed proper.

No claims of the present application are allowed.

5-[2-ethoxy-5-(4-methyl-1-piperazinylsulphonyl)-phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one is also known as sildenafil (see Applicant's disclosure at page 1, lines 12-13).

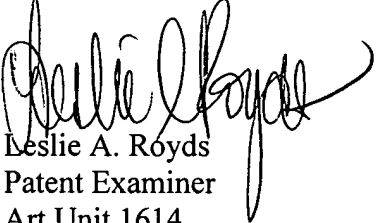
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (8:30 AM-6:00 PM), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Leslie A. Royds
Patent Examiner
Art Unit 1614

August 30, 2005



CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600